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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,538	05/03/2001	Brita Schulze	047664-5002-US	4013

9629 7590 04/02/2004

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EXAMINER	
WELLS, LAUREN Q	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,538	SCHULZE ET AL.	
	Examiner	Art Unit	
	Lauren Q Wells	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,6,10-19,26,27,32,33 and 35-52* is/are pending in the application.

4a) Of the above claim(s) *1,2,5,6,10-19,26,27,32,35 and 37-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33,36 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2, 5-6, 10-19, 26-27, 32-33, and 35-52 are pending. The Amendment filed 11/13/03, cancelled claims 3-4, 7-9, 20-25, 28-31, and 34, and added claims 35-52. Claims 1-2, 5-6, 10-19, 26-27, 32, 35, 37-51 are withdrawn from consideration, as they are directed toward non-elected subject matter.

Election/Restrictions

Applicant's election with traverse of Group V in the Response to the Restriction Requirement filed 11/13/03, is acknowledged. The traversal is on the ground(s) that "New claims 37-51 are directed to compositions comprising an agent obtained by the method of claim 36. The agents in the compositions of claims 37-51 can only be made by the method of claim 36". This is not found persuasive because claims 37-51 are directed toward compositions, whereas claims 36 and 52 are directed toward a method of modifying an agent, wherein the agent is an ingredient in a composition.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) The phrase "wherein the composition is selected from the group of particles. . .liposomes", in claim 36, and the phrase "wherein the composition is selected from the group of

molecules. . .and magnetosomes", in claim 52, are vague and indefinite, as they are confusing. How are particles, liposomes, molecules, and magnetosomes, compositions? Are they not ingredients in compositions?

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Watts et al. (5,840,341).

Watts et al. is directed toward a drug delivery composition containing chitosan or derivatives thereof having a defined zeta potential, see title. See Col. 3, line 65-Col. 4, line 8, for a method of determining zeta potential. Col. 3 specifically teaches the zeta potential being determined at pH 7.4 and 0.1M ionic strength, wherein Col. 4, lines 20-23 teach ionic strength as a solution of KCl. Col. 6, lines 48-51, teach that the conditions for carrying out the cross-linking, such as the amount of cross-linking agent required (in combination with chitosan), are determined by monitoring the zeta potential and adjusting the conditions until the required zeta potential is obtained. Claim 13 in Col. 14, lines 10-21, teaches a method of delivering a pharmacologically active compound across a mucosal surface comprising administering a composition to the mucosal surface, wherein the composition comprises a pharmacologically active compound and particles of chitosan, wherein the particles are either solidified or partially cross-linked such that they have a zeta potential of +0.5-+50mV at pH 7.4 and 0.1M ionic strength. Thus, Watts et al. disclose a method of identifying an optimal range of zeta potential (+0.5-+50mV) for a composition for targeting to a specific site (across a mucosal surface) comprising evaluating zeta potential for the composition, wherein the composition is associated

with different amounts of a cationic component (cross-linked chitosan), and identifying the optimal range of zeta potential.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watts et al. (5,840,341).

The instant invention is directed toward a method of modifying an agent to enhance its efficacy comprising associating cationic components with the agent to produce a composition having an optimal range of zeta potential for specific targeting to an activated vascular sight, wherein the composition is selected from the group of particles, liposomes, and o/w or microemulsions, or wherein the composition is selected from molecules or magnetosomes.

Watts et al. is directed toward a drug delivery composition containing chitosan or derivatives thereof having a defined zeta potential, see title. See Col. 3, line 65-Col. 4, line 8, for a method of determining zeta potential. Col. 3 specifically teaches the zeta potential being determined at pH 7.4 and 0.1M ionic strength, wherein Col. 4, lines 20-23 teach ionic strength as a solution of KCl. Col. 6, lines 48-51, teach that the conditions for carrying out the cross-linking, such as the amount of cross-linking agent required (in combination with chitosan), are determined by monitoring the zeta potential and adjusting the conditions until the required zeta

potential is obtained. Claim 13 in Col. 14, lines 10-21, teaches a method of delivering a pharmacologically active compound across a mucosal surface comprising administering a composition to the mucosal surface, wherein the composition comprises a pharmacologically active compound and particles of chitosan, wherein the particles are either solidified or partially cross-linked such that they have a zeta potential of +0.5-+50mV at pH 7.4 and 0.1M ionic strength (isoelectric point above 7.5). Thus, Watts et al. disclose a method of identifying an optimal range of zeta potential (+0.5-+50mV) for a composition for targeting to a specific site (across a mucosal surface) comprising evaluating zeta potential for the composition, wherein the composition is associated with different amounts of a cationic component (cross-linked chitosan), and identifying the optimal range of zeta potential. The reference does not teach an activated vascular site. However, the reference does teach nitroglycerine (Col. 7, line 21) as a pharmacologically active agent for use in the invention, wherein nitroglycerine acts on activated vascular sites, and does teach cardiotonics such as digitalis and digoxin as pharmacologically active agents.

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to exemplify nitroglycerine or the cardiotonics as the pharmacologically active agent in the method of Col. 14 of Watts et al., because Watts et al. teach nitroglycerine and cardiotonics as pharmacologically active agents in their invention and because of the expectation of achieving improved uptake of the agents and hence, a more potent and efficient method of treating vascular disorders.

It is respectfully pointed out that the phrase "about 0.05mM KCl solution and about pH 7.5" in claims 36 and 52 is interpreted to include 0.001mM KCl solution and pH of 7.4, as taught by the instant reference.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is 571-272-0634. The examiner can normally be reached on M&R (5:30-4).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

lqw

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER